REMARKS

I. The Office Action

The Office recognized Applicants' election of claims 1-13 and 19, as those claims are directed to a carrier for diagnosis and/or follow-up of a Treponema infection, the carrier comprising (i) at least one immobilized cardiolipin and (ii) the Treponema pallidum-specific 47 kD antigen, for further prosecution in the instant application.

The Office also acknowledged that the Information Disclosure Statement of April 20, 2007, has been considered, although documents B1, B2, and C10 were not considered because English translations were not provided. Submitted herewith are English abstracts of the relevant portions of B1 and B2, which are foreign patent documents, along with an SB/08 form listing the two references. The examiner is respectfully requested to indicate that B1 and B2 have been considered by initialing the enclosed SB/08 form and returning it to the applicants.

The Office requested that Applicants review the specification for trademarks. Applicants have amended the specification at page 11 to properly recognize a trademarks recited there.

The Office objected claims 1-3, 5-13, and 19 for being drawn, in part, to non-elected subject matter; claims 2 and 3 for reciting an acronym; and claims 5, 10, and 13 for assertedly containing "confusing" Markush language. Claim 13 was rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking written description. Claims 3, 5-9, 11-13, and 19 were rejected under 35 U.S.C. § 112, second paragraph, for alleged indefiniteness. Claims 1-3, 5-12, and 19 were rejected under 35 U.S.C. § 103(a) for allegedly being unpatentable in view of West et al., *Sex Transm. Inf.*, *78*, 282-285 (2002) ("the West reference") taken in view of Egglestone et al., *Communicable Dis. Pub. Health*, *3*, 158-162 (2000) ("the Egglestone reference") and/or Zarakolu et al., *J. Clin. Microbiol.*, *40*, 3064-3065 (2002) ("the Zarakolu reference") taken in view of Sambri et al., *Clin. Diag. Lab. Immunol.*, *8*, 534-539 (2001) ("the Sambri reference"). Reconsideration of these rejections is hereby requested.

II. The Amendments to the Claims Render Moot Many of the Objections/Rejections.

Claims 2-15, 18, and 19 have been amended, and new claims 21-30 have been added.

The new claims are each directed to an embodiment of a parent claim that was specified in the parent claim using "alternative" or "preferred" language. (The language has been stricken from the parent claims.) This use of new dependent claims better conforms the application to U.S. practice, renders moot various objections/rejections, and is not intended to narrow the scope of the subject matter claimed. Likewise, dependent method claims 14-18 have been rewritten in more conventional U.S. format.

Additionally, claim 2 has been amended to spell out an abbreviated term ("Venereal Disease Research Laboratory" = VDRL) as suggested by the Office. The claim is supported by the specification at, e.g., page 1, paragraph 6.

Claim 6 has been amended to recite that the carrier further comprises controls (as suggested by the Examiner at page 5 of the Office Action), and claims 7 and 8 have been amended to recite that the carrier comprises a serum control or a carrier control, respectively. Amended claims 6-8 are supported by the specification at, e.g., page 4, paragraph 7.

Claim 10 has been amended to better identify the Markush group recited therein.

Claims 11 and 12 have been amended to clarify that the carrier is a test strip or immunoblot, rendering moot allegations of indefiniteness.

Claim 19 has been amended to correct antecedent basis.

No new matter has been added by way of the claim amendments and additions. Applicants reserve the right to pursue the subject matter of any claim previously presented in a divisional application.

These amendments are believed to render moot all objections or rejections relating to informalities or indefiniteness.

III. The Restriction Requirement Should Be Withdrawn.

The Examiner alleges that the subject matter of claims 1 to 20 fails to meet the requirements of unity, and requires canceling method claims and limiting product claims to those "carriers in which one of the species antigens of the Treponema specific antigens" is selected. The Applicants respectfully traverse. Although the restriction has been made "final," the Examiner has cited, for the first time, new combinations of documents in support of the restriction, to which the Applicants have been given no opportunity to respond. Thus, finality of the restriction is premature, and narrowing of the claims for alleged lack of unity is premature.

The Examiner argues that a combination of VDRL antigen (cardiolipin based antigen) and Treponema based antigen on a carrier is not sufficient to establish unity, asserting that combining these ingredients on a single carrier is allegedly obvious in view of the West reference. The Examiner asserts that, in the West reference, a cardiolipin-based test ("RPR-test") is disclosed in which cardiolipin is immobilized on a coal particle. The Examiner alleges that West teaches that this cardiolipin test and a Treponema based test may be combined and for each of these tests a test employing a carrier is established. The Examiner purports to substantiate these positions by providing instruction sheets of two different RPR tests, one from Omega Diagnostics and one from Becton Dickinson.

In fact, the West reference DOES NOT teach a test system in which cardiolipin antigens are provided on a carrier. The RPR test in West et al. is a test obtainable from Quorum Diagnostics. The Examiner speculates that the RPR tests from Becton Dickinson and Omega, respectively, are suitable to prove that the RPR test from Quorum Diagnostics employs a cardiolipin antigen on a carrier. Such speculation is not a basis for establishing lack of unity.

Morover, the RPR tests as shown in the test sheets by Becton Dickinson and Omega do not employ any carrier. The Omega test sheet explains

> IMMUTREP RPR is a modified form of IMMUTREP VDRL antigen which contains carbon particles to improve visual reading of the result. When binding occurs between cholesterol/cardiolipin/lecithin in the reagant and the reagin antibodies in the sample, the results can be seen microscopically in the form of black clumps. No visual flocculation indicates a negative result.

Similarly, the BD test employs a suspension of coal particles and cardiolipin-lecithin-coated cholesterol particles which "flocculate" upon binding to anti-cardiolipin antibodies (see "Principle of the Procedure").

Accordingly, the reagin employed in RPR tests is not a coal *carrier* on which the antigen is immobilized, but rather, a suspension employing car-coal particles (see e.g. section "Reagins" of the Becton Dickinson (BD) test sheet) and VDRL antigen particles. The coal particles just increase the absorptivity of the formed antigen-antibody complex by causing a "flocculation," i.e., by the formation of black coal clumps which can be microscopically seen.

In summary, the evidence cited by the Examiner supports a conclusion of unity, as originally asserted by the applicants. The RPR test systems presented by the Examiner do not employ any carrier of the VDRL antigen. This antigen is present in a suspension capable of forming macroscopic particles with car-coal. Moreover, as explained below in greater detail, there is no prior art suggesting a test which employs both a Treponema antigen as well as a cardiolipin antigen on a single carrier.

For all of these reasons, the restriction alleging lack of unity should be withdrawn.

IV. The Rejection under 35 U.S.C. § 112, First Paragraph, Should Be Withdrawn.

The Office rejected claim 13 under Section 112, first paragraph, for allegedly lacking written description. The rejection is respectfully traversed.

Claim 13 is directed to a carrier for diagnosis and/or follow-up of a Treponema infection, comprising immobilized Treponema-specific 47 kD antigen and at least one immobilized cardiolipin presented as VDRL antigen, wherein the VDRL antigen applied to the carrier allows a differentiation between IgG and IgM antibodies directed to VDRL. The claimed subject matter is clearly described in the instant application at, for example, page 7, paragraph 1. In addition, Figures 4 and 5 depict a carrier that allow detection of IgG and IgM antibody classes. Thus, specification conveys with reasonable clarity to those skilled in the art that Applicants possessed the claimed invention as of the filing of the application, thereby satisfying the written description requirement of Section 112. *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991).

The Examiner alleges that various immunoassay steps "standard in the art" are required to differentiate between the IgG and IgM antibodies. Even if this allegation is true, it does not support a written description rejection. What is determinative in this case is that the application describes a carrier designed in a manner that allows the user to differentiate between IgG and IgM. It is conceded that the carrier described in the application is achieves this (using standard techniques), so the rejection should be withdrawn.

V. The Rejection under 35 U.S.C. § 103(a) Should Be Withdrawn.

Claims 1, 2, 5, 6, 10, 11, and 19 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious in view of the West reference taken with the Egglestone reference. Claims 1-3, 5-12, and 19 were rejected under Section 103(a) as allegedly being obvious in view of the Zarakolu reference taken with the Sambri reference. This rejection is traversed for the reasons set for the below.

The West and Egglestone References

According to the Office, the West reference discloses two possible tests for detecting Treponema infection, namely an RPR test (against VDRL) and an RST test (against a Treponema antigen). The RPR test assertedly contains cardiolipin, lecithin, and cholesterol immobilized on coal particles, while the RST test assertedly includes a 47 kD *Treponema pallidum* antigen immobilized on a carrier. The Office acknowledged that the West reference fails to disclose (a) a single carrier comprising both immobilized VDRL antigen (i.e., the cardiolipin antigen) and immobilized 47 kD antigen, (b) a carrier made of nitrocellulose,

PVDF, nylon, cellulose, acetate, or polystyrene, or (c) a test kit including instructions. The Office contends that the Egglestone reference cures the deficiencies of the West reference by allegedly recommending combining a Treponemal immunoassay with a non-treponemal test. Applicants respectfully submit that the Office's interpretation of the cited references, as well as the conclusions drawn therefrom, are incorrect.

First, the RPR test described by the West reference does not employ a carrier. The IMMUTREP RPR product sheet, provided by the Office, states

> IMMUTREP RPR is a modified form of IMMUTREP VDRL antigen which contains carbon particles to improve visual reading of the result. When binding occurs between cholesterol/cardiolipin/lecithin in the reagent and the reagin antibodies in the sample, the results can be seen microscopically in the form of black clumps. No visual flocculation indicates a negative result.

Likewise, the Becton Dickinson MACRO-VUE RPR Card Tests product sheet describes the assay as employing a suspension of coal particles and cardiolipin-lecithin-coated cholesterol particles which "flocculate" upon binding to anti-cardiolipin antibodies (see "Principles of the Procedure" and "Reagent"). Accordingly, neither West nor the secondary documents cited in the rejection support a finding that West teaches a coal carrier on which the antigen is immobilized. Rather, the prior art tests employ a suspension comprising charcoal particles and VDRL antigen particles. The coal particles increase the absorptivity of the formed antigen-antibody complex by causing a "flocculation," i.e., by the formation of black coal clumps which can be microscopically seen.

The lipid structure of cardiolipin is a labile 3-dimensional structure (forming 3-dimensional epitopes). Binding this structure to a carrier while maintaining its reactivity to anti-cardiolipin antibodies is not trivial, and is not taught by West.

The Egglestone reference merely provides an overview of possible means for detecting syphilis, and does not suggest creating a *single* carrier comprising both an immobilized Treponema-specific 47 kD antigen and at least one immobilized cardiolipin. In fact, the reference teaches away from the rejection. Looking to the Figure on page 161, the

reference suggests performing *multiple, separate* assays, i.e., primarily screening for Treponema antibodies, and later confirming infection via a VDRL test. If a sample tests positive, another Treponema test is suggested, followed by another quantitative VDRL analysis and another confirmatory test. The reference fails to suggest (or enable) performing the two assays concurrently, much less using a single carrier.

Furthermore, one of ordinary skill in the art would not be motivated to combine the RPR and RST tests described in the West reference because the assays require different test procedures, different storage, different conservation substances, and the like. Indeed, applying cardiolipin antigen and Treponema antigen on a single carrier, while allowing both antigens to be processed in such a way as to allow anti-Treponema antibody detection and anti-cardiolipin antigen detection, is not trivial. Page 1 of the Appendix shows a test strip employing VDRL and Treponema-specific antigens in which an ordinary buffer system for immunoassays is employed (0.05% TWEEN). VDRL bands are not detectable under reaction conditions suitable for Treponema antigens. Only under particular conditions do both VDRL and Treponema-specific antigens reliably show reactivity, as shown on page 2 of the Appendix. Here the concentration of TWEEN is 0.01%, which is a 50-fold reduction as compared to page 1 of the Appendix. In addition, a spatial resolution of both antigens on one carrier enabling a simple test system is not suggested by either reference. One of ordinary skill in the art would not have expected to be able to process and detect both Treponema-specific 47 kD antigen and cardiolipin antigen on the same carrier before the invention was made.

The combination of the West reference and the Egglestone reference does not suggest the "one carrier solution" of the invention, nor was there a reasonable expectation of success for providing such a carrier for the simultaneous processing and detection of cardiolipin and Treponema antigens. Thus, the cited references do not render the claimed subject matter obvious, and the rejection should be withdrawn.

The Zarakolu and Sambri References

According to the Office, the Zarakolu reference discloses an immunochromatographic tests strip comprising the Treponema 47 kD antigen and mentions

that syphilis testing generally includes non-Treponemal tests and tests for Treponemal antigens. The Zarakolu reference does not teach a carrier comprising both a cardiolipin antigen and the 47 kD antigen, does not teach application of cardiolipin at varying concentrations on the carrier, does not teach an immunoblot design, and does not teach a test kit further comprising instructions. The Sambri reference assertedly discloses a Western blot test wherein test strips comprise different antigens in different locations on the strip. The Office contends that it would be obvious to use the VDRL antigen on the Zarakolu reference's test strip because of "ease of use and because both tests are generally used in the diagnosis of syphilis."

The Zarakolu reference merely represents a first "success" in the field in providing a test strip system suitable for detecting Treponema infection. However, this test strip only employs one Treponema antigen. The Sambri test strip only contains Treponema antigens. The combination of the Zarakolu and Sambri disclosures do not point to employing different kinds of molecules (proteins and lipids such as Treponema antigens and cardiolipin, respectively) on a same carrier, resulting in a simple to handle and reliable test system for Treponema infection. There is simply no suggestion in either reference to produce a single carrier comprising both Treponema antigen and VDRL antigen. Although both tests are used to diagnose syphilis, it would not be apparent that a carrier comprising both Treponema antigen and VDRL antigen would be functional, much less "easy to use." Treponema antigen assays in the cited art require different test procedures, different storage, and different conservation substances compared to cardiolipin assays in other cited art. Furthermore, as noted above, creating an assay that allows Treponema and non-Trepomena antigens to be processed and detected is not trivial. It was not predictable that Treponema and non-Trepomena antigen detection could be achieved using a single carrier.

The cited references do not suggest the inventive carrier, and there was no reasonable expectation of success for providing such a carrier for the simultaneous processing and detection of cardiolipin and Treponema antigens. The combination of the Zarakolu and Sambri disclosures do not render the claimed subject matter obvious, and the rejection should be withdrawn.

VI. Conclusion

In view of the above amendment, Applicants believe the pending application is in condition for allowance.

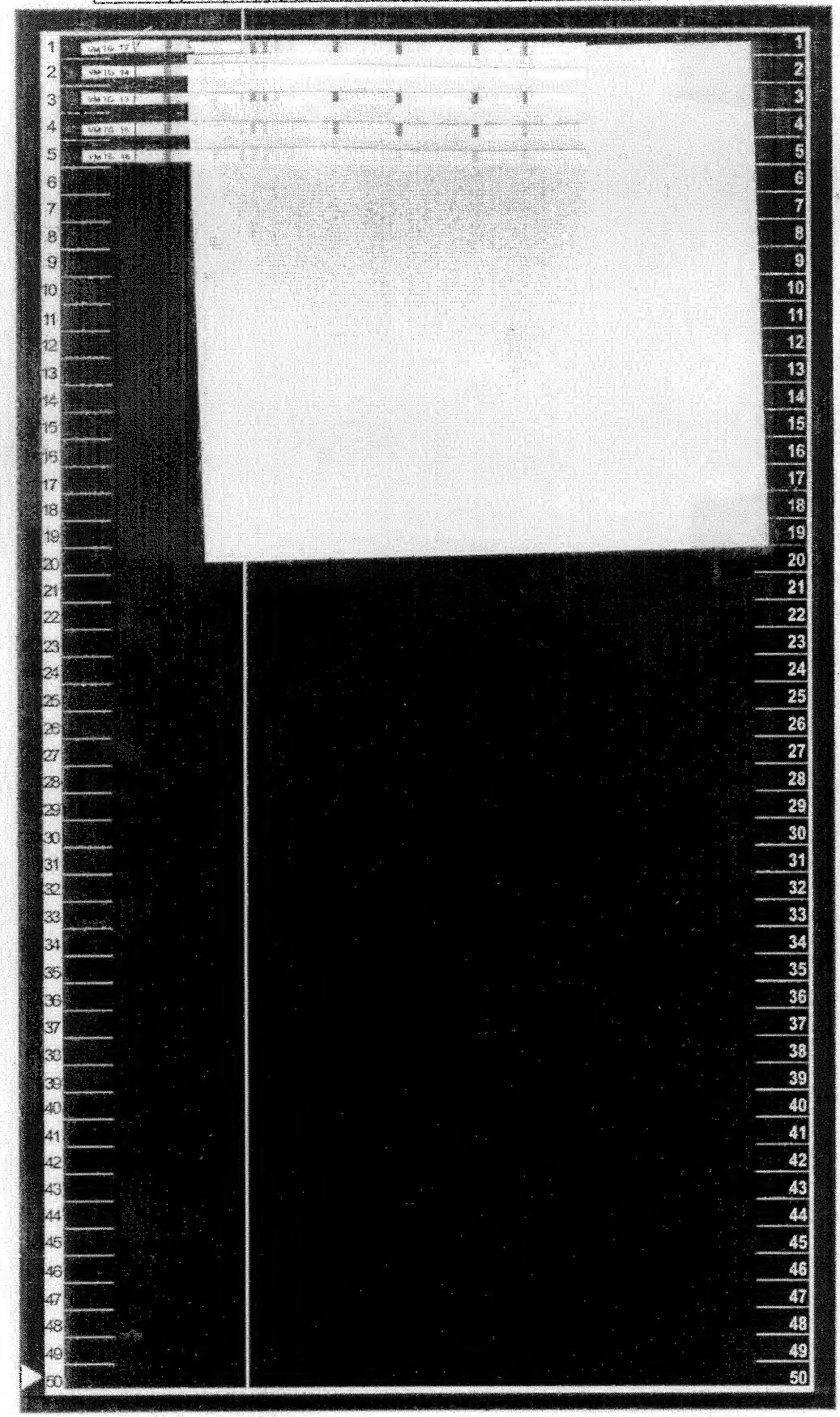
Dated: May 5, 2008

Respectfully submitted,

By _____
Heather R. Kissling
Registration No.: 45,790
MARSHALL, GERSTEIN & BORUN LLP
233 S. Wacker Drive, Suite 6300
Sears Tower
Chicago, Illinois 60606-6357
(312) 474-6300
Attorney for Applicant

ViraStripe®

IgG-Membran + VDRL, geblockt ohne Tween, entw. 0001% Tween, anti-IgG, 29.10.02



VM 546, V.+, IgG+, IgM+
VM 1332, V.-, IgG-, IgM-
BD VDRL +
BD VDRL +/-
BD VDRL -

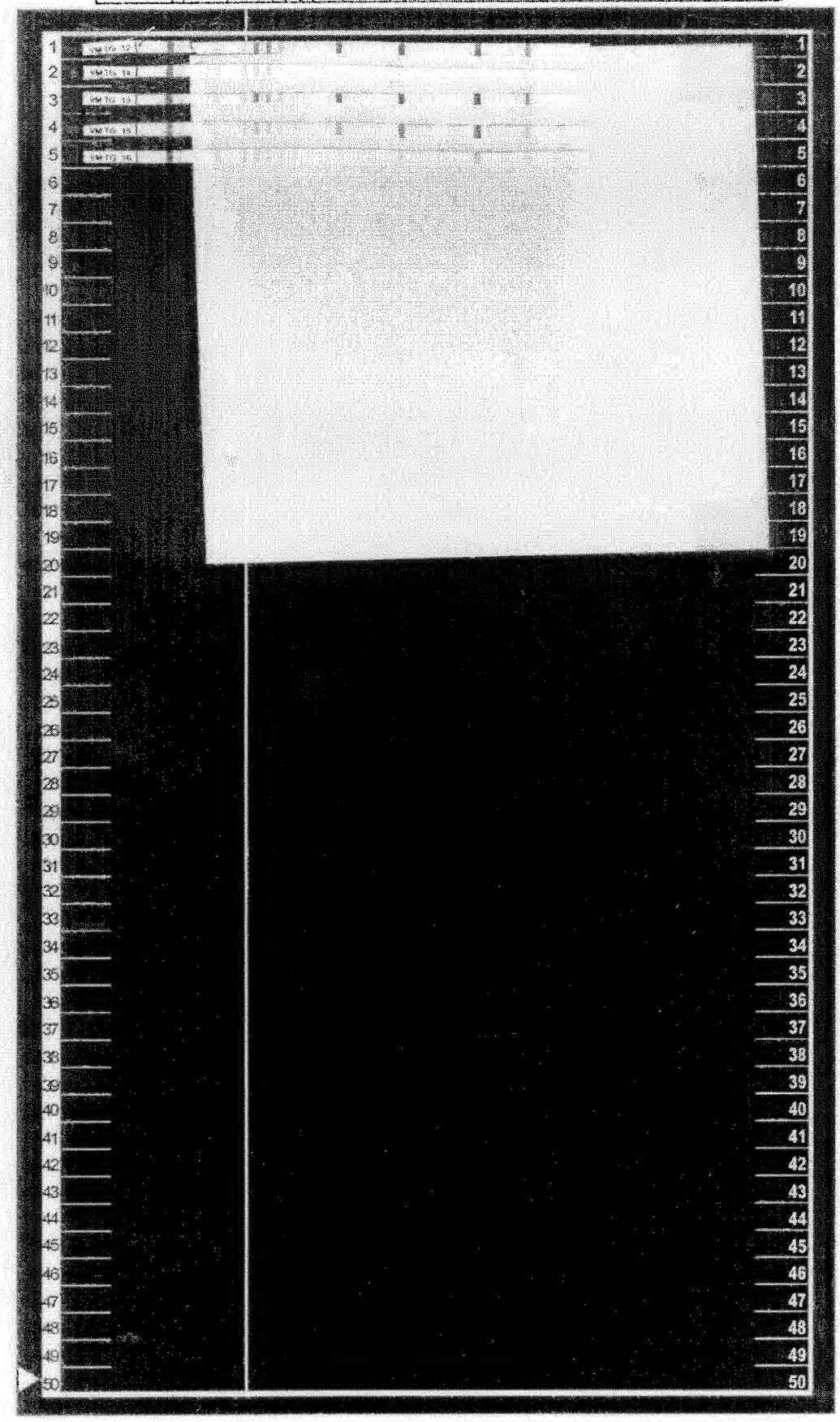
Datum: 25.10.02 Kit Ch.-Bez.-Nr. _____ Antigen Ch.-Bez.-Nr. _____ Temperatur: 23°C Entwicklungszeit: 20' IgG X IgM ___ IgA ___

APPENDIX PAGE 1

H. gentinger/ auf 'Srv-viramed'/Treponema IgM/Experimentelles/AuswertungStripes.cdr

ViraStripe®

IgG-Membran + VDRL, geblockt ohne Tween, entw. 0001% Tween, anti-IgG, 29.10.02



VM 546, V.+, IgG+, IgM+
VM 1332, V.-, IgG-, IgM-
BD VDRL +
BD VDRL +/-
BD VDRL -

Datum: 29.10.02 Kit Ch.-Bez.-Nr. _____ Antigen Ch.-Bez.-Nr. _____ Temperatur: 23°C Entwicklungszeit: 10' IgG X IgM ___ IgA ___

APPENDIX PAGE 2

H. gehringer auf 'Srv-viramed /Treponema IgM/Experimenteiles/AuswertungStripes.cdr